UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,076	11/08/1999	DENISA D. WAGNER	10861/011003	6116

28120 7590 03/22/2005

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,076	WAGNER ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/18/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,41,49-52,59,60 and 73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-41, 49-52, 59-60, 73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 11/18/04, has been entered.

Claims 40-41, 49-52, 59-60 and 73 are pending

Claims 1-39, 42-48, 53-58, 61-72 and 74 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 11/18/04.
The rejections of record can be found in the previous Office Actions.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

3. Claims 40-41, 49-52, 59-60 and 73 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description encompassing Aand another molecule≅ because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of said "molecule", are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Applicant's arguments, filed 11/18/04, have been fully considered but are not found convincing essentially for the reasons of record.

Again, page 9, lines 1-9, of the instant specification only discloses soluble forms of P-selectin or ligand including chimeric constructs between at least a portion of P-selectin or ligand and "other molecules".
It was noted that the specification discloses that soluble forms of PSGL are described in Sako et al. (Cell 75: 1179-1186, 1993).
However, there appears insufficient written description as to structure as well as function of said "other molecules" in the specification as filed.

Applicant submits that the instant claims are all drawn to methods that utilize chimeric constructs comprising PSGL-1 in combination with another molecule and that the claims state that the chimeric constructs are capable of inhibiting the interaction of P-selectin and a P-selectin ligand. Applicant also relies upon a description of the soluble forms of P-selectin on pages 8-9 of the instant specification.

However, applicant has not pointed out a sufficient written description of "another molecule" in the specification as filed.
For example, page 9, lines 1-6 of the instant specification discloses:
"Soluble forms of P-selectin or ligand are also meant to include, e.g. truncated soluble secreted forms, proteolytic fragments, other fragments and chimeric constructs between at least a portion of P-selectin or ligand and other molecules."

Beyond this sentence on page 9 of the specification as filed, the instant application does not appear to provide a sufficien written description concerning the recitation of "and other molecules".

While applicant addresses the written description of the PSGL-1 component of the claimed soluble chimeric constructs, applicant does not appear to address the "and other molecules" component of the claimed soluble chimeric constructs.

Applicant is relying upon certain biological activities of the entire chimeric construct and the structure of the P-selectin ligand element of the chimeric construct to support the broad genus of "and another molecule". The instant specification does not provide sufficient written description as to the structural features of said Aanother molecule" employed in the claimed chimeric constructs as currently encompassed by the claims. Also, the specification does not provide for the correlation between the chemical structure and the function of the genus of "another molecules", currently encompassed by the claimed invention. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biology, expression and activities. The specification as filed does not provide sufficient written description either for structurally related or unrelated "another molecules" encompassed by the claimed invention.

A person of skill in the art would not know which "another molecules" are essential or non-essential to the use of the chimeric constructs in the claimed methods based upon the disclosure in the specification as filed

Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

The instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure to support the genus of "another molecule" in the chimeric PSGL constructs employed in the claimed methods. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of "another molecule", the specification does not provide sufficient written description for the genus of "another molecule" currently claimed.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of "another molecule"; one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Id. at 1566, 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). Also see Enzo-Biochem v. Gen-Probe 01-1230 (CAFC 2002).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant's arguments have not been found persuasive.

4. Claims 40-41, 49-52, 59-60 and 73 stand rejected under 35 U.S.C. ∋ 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 6,309,639) in view of Tedder et al. (U.S. Patent No. 5,834,425), Coller et al. (U.S. Patent No. 5,976,532) and Sluiter et al. (J. Cardiovascular Pharmacology 22 (Suppl. 4): S37-S44, 1993) essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record and reiterated herein for applicant's convenience.

Applicant's arguments, filed 11/18/04, have been fully considered but are not found convincing essentially for the reasons of record.

For a more complete analysis of applicant's arguments and the examiner's rebuttal on the 1.131 declaration and references of record, see the previous Office Action, mailed 7/14/04.

Applicant's arguments in conjunction with the 1.131 declaration under 37 C.F.R. 1.131, filed 5/4/04, have been fully considered but are not found convincing essentially for the reasons of record.

With respect to the applicant's reliance upon applicant's 131 Declaration and Exhibits of record to antedate the prior art, the following of record is noted.

Absent a clear support or facts are establishing applicant's assertions of conception and diligence (and reduction to practice or subsequent reduction to practice) before the prior art, applicant's arguments have not been found persuasive and the rejection is maintained for the reasons of record.

Applicant agrees that the information supplied in the declaration does not relate directly to restenosis, however, since the Cummings et al. references does not relate to restenosis, it is entirely unnecessary to antedate Cummings as it applies to claim 73.

For the reasons of record, the prior art of record meets the claimed limitations, including claim 73.

Applicant asserts that the Sluiter et al. reference speculates that granulocyte and/or monocytes may play a role in contributory role in the pathogenesis of coronary restenosis following balloon angioplasty but asserts that there is no confirming data or other disclosure that would lead one skilled in the art to attempt to use a PSGL-1 chimera to treat atherosclerosis or restenosis.

In contrast to applicant's characterization of Sluiter,et al., again, Sluiter et al. was provided to add further evidence that the ordinary artisan would have targeted the inhibition of P-selectin-mediated events in therapeutic strategies of inhibiting leukocyte adhesion receptors to alleviate tissue damage in cardiovascular diseases (see entire document, including Figure 1 and Table 1), including those patients suffering from heart attack, atherosclerosis and coronary restenosis (see Concluding Remarks on page S42).

The Concluding Remarks on page S42 of Sluiter et al. state:
"The rapidly growing knowledge about the mechanisms that underly the adherence of granulocytes and monocytes to the endothelium will soon provide cardiologists with new drugs to treat their patients suffering from hear attach, atherosclerosis and coronary restenosis. Those drugs will be targeted to relevant inflammatory mediators, leukocyte adhesion molecules expressed by activated endothelium and signaling pathways involved in their expression, inhibiting the extravasation of more of those leukocytes that otherwise exacerbate tissue damage."

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(C).

Again, applicant asserts that Cummings et al. is directed to treating the inflammatory conditions resulting from the rupture of atherosclerotic lesions or plaque occurring which after the disease (atherosclerosis) has progressed to its end stages (see column 19, lines 57-64), which is distinct from the claimed methods directed to preventing the formation or growth of atherosclerotic lesions (i.e. conditions leading to the development of atherosclerosis).

However, the combination of references does provide sufficient motivation and expectation of success in providing chimeric PSGL-1 to treat various disorders and conditions associated with platelet-leukocyte interactions including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, encompassed by the claimed methods. For example, see Clinical Applications on columns 18-22 and Claims of Cummings et al. Cummings et al. also teach that both acute and chronic disorders are targeted therapies (see column 18, paragraph 5) as well as the pathological situations arising from issue damage resulting from leukocytes associated with ischemia and reperfusion as well as clinical cardiology (see columns 18, paragraphs 6-7 to column 19, paragraph 1).

Given the prior art teachings supporting methods of treating artherosclerosis as well as treating patients undergoing vessel-corrective techniques, decreasing the formation or growth of atherosclerotic lesions as well as treating or inhibiting atherosclerosis would have been an expected or intrinsic property of treating patients undergoing vessel-corrective techniques with PSGL-1.

Again, applicant acknowledges that Tedder et al. discloses that chimeric peptides can be formed from different selectins but asserts that applicant is claiming a method of using certain chimeric molecules to treat atherosclerosis and restenosis..

As pointed out previously, Tedder et al. teach the art known generation and use of chimeric peptides combining ligand binding portions of selecting based inhibitory therapeutics, including those based upon P-selectin, with other molecules such as immunoglobulin to increase serum half-life or avidity of the therapeutic agent to block platelet or leukocyte-mediated inflammation (see entire document, including Use on columns 10-14). Similar to Cummings et al. and art known practice at the time the invention was made, Tedder et al. teach combination therapy (see column 13, paragraph 1).

Given the art known practice and desire to increase the avidity and/or half-life of therapeutics in general, including selectin-mediated inhibitors, as taught by Tedder et al., one of ordinary skill in the art would have been motivated to modify the PSGL-1 and fragments thereof taught by Cummings et al. By making chimeric constructs thereof in the treatment of cardiovascular disorders.

Again, applicant asserts that there is no motivation to combine Coller et al. with Cummings et al. because Cummings et al. does not mention surgical procedures or chimeric molecules and Cummings et al. / Tedder et al. are directed to inflammatory conditions which are not discussed in Coller et al.

Again, Cummings et al. teach the clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, by inhibiting platelet-leukocyte interactions with PSGL-1 and fragments thereof (see entire document, including Clinical Applications on columns 18-22 and Claims). Cummings et al. teach that the therapeutic use that reduce leukocyte adherence in ischemic myocardium can significantly enhance the therapy efficacy of thrombolytic agents (see column 18, paragraph 7).

Also, as pointed out previously, Coller et al. teach the art known vessel-corrective techniques at the time the invention was made in the treatment of cardiovascular disorders such as atherosclerosis and reocclusion, including angioplasty, atherectomy and coronary bypass surgery (see Background of the Invention on column 1 and Utility of Platelet-specific Chimeric Immunoglobulin on columns 5-7). In teaching the use of an inhibitor of platelet aggregation and thrombus formation associated with such conditions, Coller et al. teach the art known use of combination therapy with other drugs such as thrombolytic agents and that the amounts administered before, along with or subsequent to treatment will depend on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made (see column 6, paragraphs 2-3). Coller et al. teach that antibodies reactive with platelets, including antibodies that bind GMP-140 (i.e. P-selectin) can be used (see column 3, paragraph 3). Therefore, the prior art does teach targeting P-selectin in the context of vessel-corrective procedures.

As pointed out previously and in contrast to applicant's assertions, Cummings et al. and Coller et al. are drawn to the same or similar methods of inhibiting platelet-leukocyte / endothelial interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury as well as cardiovascular disorders such as atherosclerosis and restenosis, including angioplasty, atherectomy and coronary bypass surgery.

Given the art known practice of combination therapy, as taught by Cummings et al., Tedder et al. and Coller et al. as well as the art known practice of vessel-occlusive techniques to treat atherosclerosis and restenosis, as taught by Coller et al., one of ordinary skill in the art would have been motivated to administer the PSGL-1 and fragments thereof, as taught by Cummings et al. in various vessel-occlusive techniques given its properties of inhibiting platelet-leukocyte interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, as taught by Cummings et al. with an expectation of success.

Given the art known practice of modes of administrations and dosing depending on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made, as taught by Coller et al. In cardiovascular diseases, the claimed limitations were met or would have been obvious variants in meeting the needs of the patients in order to achieve a therapeutic effect depending on the symptom at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's arguments have not been found persuasive.

5. No claim is allowed.

6. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
March 14, 2005